(e) contracting a second biomolecule with the mass-coded combinatorial library, whereby members of the mass-coded combinatorial library which are ligands for the second biomolecule bind to the second biomolecule to form second biomolecule-ligand complexes;

(f) separating the second biomolecule-ligand complexes from the unbound members of the mass-coded combinatorial library;

(g) dissociating the second biomolecule-ligand complexes;

(h) determining the molecular mass of each ligand for the second biomolecule; and

(i) determining which molecular mass or masses determined in step (d) are not determined in step (h), thereby providing the molecular masses of members of the mass-coded combinatorial library which are ligands for the biomolecule but are not ligands for the second biomolecule.

wherein each molecular mass determined in step (i) corresponds to a set of n peripheral moieties present in a ligand for the first biomolecule which is not a ligand for the second biomolecule, thereby identifying a member of the mass-coded combinatorial library which are ligands for the biomolecule but are not ligands for the second biomolecule.

55. The method of claim 54 wherein the biomolecule and the second biomolecule are each, independently, a protein or a nucleic acid molecule.

56. The method of claim 55 wherein the biomolecule and the second biomolecule are each a protein, and the amino acid sequence of the second biomolecule is derived from the amino acid sequence of the biomolecule by insertion, deletion or substitution of one or more amino acid residues.

57. The method of claim 55 wherein the biomolecule is a first protein and the second biomolecule is a second protein, said first and second proteins having the same

amino acid sequence, wherein said first and second proteins have different posttranslational modifications.

58. The method of claim 57 wherein the first protein differs from the second protein in extent of phosphorylation, glycosylation or ubiquitination.

59. The method of claim 55 wherein the second biomolecule is a complex of the biomolecule with a ligand.

60. The method of claim 55 wherein the biomolecule and the second biomolecule are each immobilized on a solid support.

61. The method of claim 60 wherein the solid support is a water-insoluble matrix contained within a chromatographic column.

62. The method of claim 55, wherein one or more of steps (b) and (f) is performed by contacting a solution comprising biomolecule-ligand complexes or second biomolecule-ligand complexes and unbound members of the mass-coded combinatorial library with a size exclusion chromatography column, whereby the unbound members of the mass-coded combinatorial library elute from the column after the biomolecule-ligand complexes or the second biomolecule-ligand complexes.

63. The method of claim 55, wherein one or both of steps (b) and (f) is performed by contacting a solution comprising biomolecule-ligand complexes or second biomolecule-ligand complexes and unbound members of the mass-coded combinatorial library with a size exclusion chromatography column, whereby the members of the mass-coded combinatorial library pass through said membrane and the biomolecule-ligand complexes or second biomolecule-ligand complexes do not pass through said membrane.

64. A method for identifying a member of a mass-coded combinatorial library which is a ligand for a first biomolecule but is not a ligand for a second biomolecule, said mass-coded combinatorial library comprising compounds of the general formula XY_n, wherein n is an integer from 2 to about 6, X is a scaffold having n

reactive groups, and each Y is, independently, a peripheral moiety, wherein each reactive group is capable of reacting with at least one peripheral moiety precursor to form covalent bond, and wherein said mass-coded combinatorial library is produce by reacting a scaffold precursor with a peripheral moiety precursor subset selected from a peripheral moiety precursor set, said peripheral moiety precursor subset comprising a sufficient number of distinct peripheral moiety precursors such that there exist at least about 250 distinct combinations of n peripheral moieties derived from said peripheral moiety precursors, wherein said subset includes at least two different peripheral moiety precursors that are each contacted with and can each react with at least two different reactive groups, said method comprising the steps of:

(a) contacting the second biomolecule with the mass-coded combinatorial library, whereby members of the mass-coded combinatorial library which are ligands for the second biomolecule bind to the second biomolecule to form second biomolecule-ligand complexes and members of the mass-coded library which are not ligands for the second biomolecule remain unbound;

(b) separating the second biomolecule-ligand complexes from the unbound members of the mass-coded combinatorial library;

(c) contacting the first biomolecule with the unbound members of the mass-coded combinatorial library of step (b), whereby members of the mass-coded combinatorial library which are ligands for the first biomolecule bind to the first biomolecule to form first biomolecule-ligand complexes and members of the mass-coded library which are not ligands for the first biomolecule remain unbound;

(d) dissociating the first biomolecule-ligand complexes;

(e) determining the molecular mass of each ligand for the first biomolecule;

wherein each molecular mass determined in step (e) corresponds to a set of n peripheral moieties present in a ligand for the first biomolecule which is not a ligand for the second biomolecule, thereby identifying a member of the mass-coded combinatorial library which is a ligand for the second biomolecule.

65. The method of claim 64 wherein the first and second biomolecules are each, independently, a protein or a nucleic acid molecule.

66. The method of claim 64 wherein the second biomolecule is immobilized on a solid support.

67. The method of Claim 66 wherein the solid support is a water-insoluble matrix contained within a chromatographic column.

68. A method for identifying a member of a mass-coded combinatorial library which is a ligand for a biomolecule and binds the biomolecule at the binding site of a known second ligand for the biomolecule, said mass-coded combinatorial library comprising compounds of the general formula XY_n, wherein in n is an integer from 2 to about 6, X is a scaffold having n reactive groups, and each Y is, independently, a peripheral moiety, wherein each reactive group is capable of reacting with at least one peripheral moiety precursor to form a covalent bond, and wherein said mass-coded combinatorial library is produced by reacting a scaffold precursor with a peripheral moiety precursor subset selected from a peripheral moiety precursor set, said peripheral moiety precursor subset comprising a sufficient number of distinct peripheral moiety precursors such that there exists at least about 250 distinct combinations of n peripheral moieties derived from said peripheral moiety precursors, wherein said subset includes at least two different peripheral moiety precursors that are each contacted with and can each react with at least two different reactive groups, said method comprising the steps of:

a) contacting the biomolecule with the mass-coded combinatorial library, whereby members of the mass-coded combinatorial library which are

ligands for the biomolecule bind to the biomolecule to form biomolecule-ligand complexes and members of the mass-coded combinatorial library which are not ligands for the biomolecule remain unbound;

b) separating the biomolecule-ligand complexes from the unbound members of the mass-coded combinatorial library;

c) contacting the biomolecule-ligand complexes with the second ligand to dissociate biomolecule-ligand complexes in which the ligand binds to the biomolecule at the binding site of the second ligand, thereby forming biomolecule-second ligand complexes and dissociated ligands;

(d) separating the dissociated ligands and biomolecule-ligand complexes; and

(e) determining the molecular mass of each dissociated ligand,

wherein the molecular mass of each dissociated ligand corresponds to a set of peripheral moieties present in that ligand, thereby identifying a member of the mass-coded combinatorial library which is a ligand for the biomolecule and binds to the biomolecule at the binding site of the known second ligand for the biomolecule.

69. The method of claim 68 wherein the second ligand is a polypeptide, a nucleic acid molecule or a cofactor.

70. The method of claim 68 wherein the biomolecule is immobilized on a solid support.

71. The method claim 70 wherein the solid support is a water-insoluble matrix contained within a chromatographic column.

72. The method of claim 68 where the biomolecule is a protein or a nucleic acid molecule.

REMARKS

Upon entry of the foregoing amendment, claims 16-22 and 51-72 are pending in the application. Support for this amendment may be found throughout the